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Late stage Cesareans cause recurrent, early preterm birth: how to tackle this problem?

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INTRODUCTION

Preterm deliveries have multiple aetiologies and management is dependent on cause.

Recent studies have shown that caesarean sections performed late in labour have been

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associated with recurrent, early premature births and late miscarriages (Figure 1). Both the prediction and management of these under-recognised high-risk cases needs to be elucidated. Along with raising awareness, further research is needed to understand aetiology and to create prevention and management strategies, particularly in light of the escalating caesarean section rate.

There are 500,000 premature deliveries under 37 weeks annually in the United States. Worldwide there are 15 million each year with associated serious health implications and high costs to families and society. The management and prevention of preterm birth is highly variable dependent on the aetiology. A recent, association, likely to be causative, has been made between caesarean delivery at full dilatation (FDCS) and caesareans performed late in labour with increased risk of early, recurrent premature birth and late miscarriage. The clinical problems that FDCS pose in subsequent pregnancies need to be highlighted as it is currently under-recognised. There needs to be further research into prevention and management strategies.

SCOPE OF THE PROBLEM

Rising rate of late dilatation caesarean sections

The caesarean section rate has escalated in recent decades in middle to high-income countries. Worldwide, caesarean rates have increased three fold (from 6.7% in 1990 to 19.1% in 2014)¹. Even in countries known for their high caesarean rates this increase continues; in the United States they have risen from 20.7% to 31.9% in 2016 over a span of 20 years²; equivalent data from the last two decades in the United Kingdom, consists of a rise from 17% to 28%^{3,4}. Of those caesarean sections performed as an emergency, up to 20% (large Australian cohort of 2672 women)⁵ have been reported to be performed at full dilatation and this proportion is increasing^{6,7,8}. This may reflect the unwillingness to perform assisted vaginal deliveries. One cohort demonstrated that 25% of all women requiring intervention in the second stage had a caesarean section⁹. In the UK, FDCS occur in approximately 5% of all caesareans performed and this represents approximately 8,000 deliveries per annum in the UK^{6,8,10}.

Complications of fully dilated Caesarean sections

Maternal and neonatal complications of FDCS are well described and include laceration of the bladder, bowel, ureter, uterine artery or extension of the uterine incision, haemorrhage with or without blood transfusion, and hysterectomy as well as fetal lacerations and

puerperal febrile episodes^{6,11}. These complications may be exacerbated with increased length of second stage.

The complication of preterm birth has now been linked to late stage caesarean sections. Levine et al., exposed a six-fold increased risk of preterm birth following FDCS¹². In their study, 13.5% of women who had FDCS had a subsequent preterm delivery compared with 2.3% in women who underwent a first stage caesarean; OR 5.8 (95%CI 1.08–30.8, $P=0.04$)¹². In addition there may be longer term impact; Watson et al. (2017) showed 53% of women with a history of FDCS experienced recurrent pregnancy losses, in spite of intervention, compared to 14% with a history of preterm birth without a FDCS as a risk factor (relative risk 3.06 95% confidence interval 1.22-7.71)¹³. Conventional treatment with vaginal cerclage did not appear to offer protection in this group who had a preterm birth following FDCS. In Watson's study, 17/29 women in the FDCS group received intervention compared to 6/37 in the control group, 55% (16/29) women in the FDCS group delivered before 37 weeks compared to 19% (7/37) in the control group¹³. Of the 38% (11/29) women with a vaginal cerclage in the FDCS group, 45% (5/11) still delivered preterm¹³.

There appears to be a continuum of risk with regards to degree of cervical dilatation at time of caesarean delivery. The relative risk (RR) of spontaneous preterm delivery prior to 32 weeks gestation in a large US study was 2.48 (95% CI, 1.77-3.49) following a caesarean at 9-10cm dilated, compared to a 1.63 when cervical dilatation was 0-4cm (95% CI, 1.44-1.85)¹⁴.

A more recent large Australian cohort study has shown an absolute risk of preterm birth following FDCS to be lower but still double compared to those with a previous first stage caesarean (1.7 vs 3.8%)⁵. Current data do not include mid-trimester losses and could be an underestimation of the risk. Mid-trimester losses represent an important outcome which needs further evaluation in the context of a prior FDCS.

HYPOTHESES OF PATHOPHYSIOLOGY

It has been suggested that cervical injury compromising the integrity of the cervix can predispose to subsequent preterm birth ^{12,13}. As the lower segment thins over the presenting part during labour, it is thought that the incision at caesarean is made inadvertently too low within the cervix or even vagina¹⁵. It is arguable that it is this incision within the cervical tissue rather than an extension of the incision into the cervix which contributes to cervical incompetence.

The difficulty of defining the border between lower uterine segment and the cervix has been well documented as early as 1939 by Marshall¹⁶. He described that at full dilatation, “the inferior limit of the lower segment can no longer be defined, by sight or touch, with absolute precision” ¹⁶. Marshall also described how the cervix or vaginal wall may be incised during a caesarean section late in labour ¹⁶. In 1980, the inferior margin of the lower segment, supra-vaginal and vaginal cervix were described as continuous at full dilatation, and there was difficulty defining the marking of the cervical-corporal junction in an effaced cervix ¹⁷. In the 1980s, inadvertent primary vaginal incisions were reported at full dilatation in the second stage¹⁷. It was only in 1996 that Iams described cases of incompetent cervix in women after a caesarean section carried out following prolonged pushing in the second stage¹⁸. This kind of trauma or laceration to the cervix was attributed to poor healing where the cervix is “stretched beyond tolerance”¹⁸.

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Prolonged second stage (without analysis of mode of delivery or cervical dilatation) has been identified by some studies as a risk factor for preterm birth^{19,20}. A second stage of labour longer than 180 minutes in a first pregnancy was associated with an 81% increased risk of preterm delivery in subsequent pregnancy (HR 1.81, 95% CI 1.15-2.84)²¹. However, Wood et al. found that a FDCS and not the duration of the second stage was associated with a higher risk of delivery before 32 weeks, suggesting that the FDCS, and not the length of the second stage, is the mechanism of preterm labour¹⁴.

Levine et al proposed that cervical extensions from the uterine incision during a FDCS increase the risk of spontaneous preterm birth¹². However, cervical extensions do not account wholly for the increased preterm birth incidence as high rates of early delivery remain even when the extension cases are excluded from the analysis (9.1% spontaneous preterm birth incidence following FDCS versus 0.9% following first stage Caesarean section, $p=0.02$)¹².

Injury to the cervical morphology during FDCS has been suggested as the mechanism of subsequent spontaneous preterm birth^{12,13,20,22}. Recent evidence suggests the cervix comprises of a specialized sphincter at the internal os composed of 50-60% circumferential

smooth muscle around the endocervical canal down to the external os which is composed of 10-15% smooth muscle²³. It has been proposed that the cervical smooth muscle cells may have a role in cervical remodelling as well as initiating and/or disseminating uterine contractility²³. This novel sphincter morphology may be a key to investigating mechanisms of premature and term cervical remodelling. It is thought that cervical effacement causes the internal sphincter smooth muscle to migrate into the lower uterine segment which can be disrupted during a FDCS²⁰ thus resulting in incomplete recovery of cervical muscular function. Furthermore, closure of the uterine defect if too low or extensions to the cervix due to difficulty delivering an impacted fetal head could equally injure the internal os²⁴.

These hypotheses underpinning FDCS and future preterm delivery are unproven. The trauma alone may not explain why over 80% of those having a FDCS do not experience a subsequent preterm birth, and there may be degrees of insult or the level of trauma could be critical. The healing processes in caesarean scars, the role of infection and/or ischaemia as well as operative technique need further consideration. This includes comparison between vertical and horizontal lower segment uterine incisions as a possible intervention, and the effect on circular sphincter competence at the internal os. Furthermore, the suture material and comparison between single and double-layer closure warrants evaluation, as this could influence ischemia and healing. Our current prediction tools such as cervical length and fibronectin testing additionally warrant further investigation in this specific population to ensure their validity.

Confounders to this new problem

Decision-making regarding the need for as well as the execution of second stage delivery requires experienced operator input. The rise of FDCS is often related to decreased success of assisted vaginal deliveries⁸. There is a fear of litigation over assisted vaginal deliveries and this has led to a decline in their use^{25,26}. FDCS may be perceived as the safer option. Deskilling of obstetric trainees in the UK influenced by working significantly fewer hours thus limiting their exposure, due to the European Working Time Directive, has also played a part in this⁶. Furthermore, the patient demographic is changing with more primiparous births occurring at a higher booking body mass index (BMI) and at increasing maternal age. It is likely similar effects are occurring in high income settings worldwide.

EVIDENCE FOR IMAGING SURVEILLANCE

There have been reports of anterior cervical defects visualized on transvaginal ultrasound of women with previous FDCS. This is not routinely looked for in antenatal ultrasound scans and their relationship to preterm birth risk is unclear¹⁶. The screening and optimum management of cervical defects needs to be further researched and resolved.

Repair of caesarean defects, known as a niche or isthmocoele, has been described in cases of subfertility, intermenstrual bleeding, dysmenorrhoea or dyspareunia. A 38 patient case series of laparoscopic repair with pre and post Magnetic Resonance Imaging (MRI) identified a significantly increased myometrial thickness following repair, which was also reproduced on histological analysis²⁷. One hypothesis regarding niche development highlights that a low cervical incision may induce the formation of “retention cysts” and presence of mucus-producing glands may hamper healing²⁸. Furthermore, a larger number of niches are associated with a shorter distance between the caesarean scar and internal os as well as with increasing cervical dilatation²⁹. Incomplete uterine closure and adhesion formation which impair healing have also been implicated in niche creation. The appearance of this niche has not been commonly linked to preterm birth, partly due to subspecialty focus in research, but has been described in case studies³⁰.

A recent study compared the added value of MRI in the analysis of Caesarean scars compared to transvaginal monitoring. MRI was able to analyse the remaining muscle fibres at the level of the scar³¹, but this has not yet been correlated with preterm birth risk in the FDCS population as it was not specifically investigating scars within the cervix. Although a caesarean scar can be identified by transvaginal ultrasound at the same time as cervical length assessment, it is limited in terms of analysing the scar morphology^{29,31}. Further work will need to establish whether imaging features by ultrasound or MRI can predict outcome, and possibly direct interventions prior to an adverse event.

EVIDENCE FOR CURRENT MANAGEMENT

Transvaginal ultrasound screening of cervical length is increasingly used to ascertain preterm birth risk. It is unknown whether this is valid with FDCS as a risk factor. Equally it is unknown which interventions may reduce risk. Decisions regarding interventions largely vary depending on clinician's expertise, experience and preference. Limited data suggest that vaginal cerclage may fail more commonly in women with this risk factor¹³. This makes physiological sense if the suture is confined to encircling the vaginal (distal) portion of the cervix. Transabdominal cerclage has been suggested as the most effective management option³⁰ but larger studies are needed to support this. One can hypothesize that a transabdominal cerclage provides support above the level of the defect caused by a low incision in the cervical tissue which logically would be the best way forward in future term pregnancy success. However, this procedure is more invasive and requires caesarean section for subsequent delivery and so identifying which women would benefit from this needs urgent clarification.

In the first instance, greater awareness by both the public and healthcare professionals of the potential risk following likely iatrogenic injury during FDCS would increase referrals, and research in the area. Prevention is better than cure; we feel the workforce should not deskill at assisted deliveries. The relative merits of a higher, or perhaps vertical, uterine incision in order to reduce the problem needs to be evaluated. In women with preterm birth following

FDCS, screening tests (biophysical and biochemical) to ascertain risk and subsequent interventions require clinical trials. In particular the role of cervical scanning and MRI in evaluating the prior cervical injury and scar would be valuable. The role of higher placed sutures should also be investigated, both vaginal and abdominal. The role of these interventions in women with and without a history of prior preterm birth events is also important, perhaps linked to prediction tests.

SUMMARY

The complications of FDCS have recently come to light and it is a sobering reminder of how our well-intentioned interventions can lead to serious harm, and the need to remain vigilant and to continually audit our current practice. It is likely more than 14% of women with a FDCS experience subsequent mid-trimester losses and/or preterm births, which is recurrent and difficult to treat. By raising awareness of this important problem, we aim to focus research efforts on optimal management as well as prevention of FDCS.

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Figure legend

Figure 1 Key data on the extent of the FDCS problem, hypothesised causes and potential solutions

Extent of the FDCS problem:

- The rate of emergency caesarean sections including FDCS are increasing with published intrapartum cohorts demonstrating up to 20% are FDCS^{5,7}
- The spontaneous preterm birth rate following FDCS is 13.5% with a six fold higher rate compared to a caesarean in the first stage of labour¹²
- A caesarean following a prolonged second stage of >3 hours likely confers double the absolute risk²⁴

Proposed mechanism:

- It is hypothesised that the FDCS insult is as a result of inadvertent incision of the cervix^{12,13,18,20}
- It is hypothesised that an injury to the cervical morphology occurs including niche formation^{22,28}

Possible solutions:

- Vaginal cerclage may fail more commonly with this risk factor¹³
- Transabdominal cerclage has been suggested as more effective³⁰